Quality of Life-Nontuberculous Mycobacteria (NTM) Module

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ACKNOWLEDGEMENTS: EMILY HENKLE, KEN OLIVIER, MATTHIAS SALATHE, KEVIN WINTHROP

Objectives

- Nontuberculous mycobacteria (NTM) is a substantial cause of pulmonary infections and can affect those with chronic respiratory diseases, such as cystic fibrosis (CF) and bronchiectasis.

- NTM is rare, poorly understood, and difficult to treat, with few clear identified endpoints to evaluate new medications in randomized, controlled trials.

- We are developing a patient-reported outcomes (PROs) that identify key symptoms, tracks the progression of disease, and can serve as an important end-point in clinical trials of new therapies (FDA Guidance, 2009)

- The aim of this study was to develop an instrument for NTM symptoms; can be used with existing PROs measures for CF (CFQ-R) and bronchiectasis (QOL-B)
Patient-Reported Outcomes: PROs

Both FDA & EMA now accept PROs as primary or secondary endpoints in clinical trials

*Treatment Benefit* = how a patient feels, functions and survives (FDA, 2009)

Begins with open-ended interviews with patients, experts; content analysis of key concepts; draft items and cognitive testing

Psychometric validation: reliability, validity, sensitivity to changes

Importantly: reflects the “*patient’s voice*”
Methods

• We followed the FDA Guidance on PROs (2009)
• Reviewed published literature on NTM to identify critical symptoms and challenges of living with NTM
• Focus groups, moderated by a psychologist, were conducted with adults with NTM + bronchiectasis at 2 sites, N=31
• A consensus panel of 9 pulmonologists with expertise in NTM provided input on how NTM and its treatment affects their patients
• Open-ended interviews were conducted with 13 patients: how NTM affects daily functioning; frequent and difficult symptoms coded in Atlas.ti
• Cognitive testing, using a standard “think aloud” procedure conducted with 53 adults; input on preliminary items & rating scales
• We completed an initial psychometric validation of the module in 148 patients
Focus groups of adults with bronchiectasis and NTM (N=31)

Focus group with medical experts treating NTM (N=9)

Open-ended interviews with patients to identify key symptoms and impact of disease on daily functioning (N=13)

Interviews coded in Atlas.ti to identify critical concepts

Instrument Created

Cognitive testing (N=53) of draft instrument to assess clarity, relevance, and completeness, administered NTM Module

NTM Module completed by total of 148 individuals – preliminary psychometric analyses completed
## Key Themes

### Main themes from Focus Groups (N=31)

- Frequent pain (dull, aches, pressure in chest)
  - Metal taste in mouth
- Fever
  - Lack of sleep

### Main themes from Open-Ended Interviews (N=13)

- Fatigue
  - Sensitivity to smell
- Sensitivity to cold/chills
  - Hot flashes/sweats

### Main themes from Physician Panel (N=9)

- Memory loss
  - Body Image issues
- Side effects from medications: GI problems
  - Weight loss with greater disease severity
Results

- Focus groups and open-ended interviews identified sleep quality, fever, and chills; physicians also identified body image as a concern.
- The new NTM Module consists of eight unique symptoms; administered to 148 patients ($\alpha = .73$); very good reliability.

Sample items from NTM module

- “Bothered by cold weather?”
- “Have you experienced problems with memory?”
### NTM Symptoms

**Indicate how you have been feeling during the past week:**

<table>
<thead>
<tr>
<th>Question</th>
<th>A lot</th>
<th>A moderate amount</th>
<th>A little</th>
<th>Not at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>46. Have you had eating problems?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>47. Have you had trouble gaining weight?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>48. Have you felt feverish (sweating, chills)?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>49. Have you had problems sleeping?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>50. Have you had pain?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>51. Have you felt bothered by cold weather?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>52. Have you had sensitivity to smell?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>53. Have you had sensitivity to taste?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>54. Have you had a bad taste in your mouth due to sputum?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>55. Have you experienced problems with memory?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>
### Internal consistency of NTM module (N = 148)

<table>
<thead>
<tr>
<th>Scale Name</th>
<th>Cronbach's Alpha</th>
</tr>
</thead>
<tbody>
<tr>
<td>NTM Symptoms</td>
<td>0.73</td>
</tr>
<tr>
<td>Body Image</td>
<td>0.76</td>
</tr>
<tr>
<td>Eating Problems</td>
<td>0.89</td>
</tr>
<tr>
<td>Digestive Symptoms</td>
<td>0.75</td>
</tr>
</tbody>
</table>
# Multitrait Analysis of NTM Module (N = 148)

<table>
<thead>
<tr>
<th>Item</th>
<th>Abbreviated Item Content</th>
<th>NTM Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>NTM48</td>
<td>Feverish (chills, sweating)</td>
<td>0.42&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>NTM49</td>
<td>Problems sleeping</td>
<td>0.39&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
<tr>
<td>NTM50</td>
<td>Pain</td>
<td>0.41&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>NTM51</td>
<td>Bothered by cold weather</td>
<td>0.51&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>NTM52</td>
<td>Sensitivity to smell</td>
<td>0.37&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
<tr>
<td>NTM53</td>
<td>Sensitivity to taste</td>
<td>0.39&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>NTM54</td>
<td>Bad taste in mouth</td>
<td>0.48&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>NTM55</td>
<td>Memory problems</td>
<td>0.45&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Item-scale correlation adjusted for overlap (item removed from its scale for correlation)

<sup>b</sup>Item-scale correlation is <.40
Algorithm for administering NTM module with QOL-B or CFQ-R

Individual with NTM

Bronchiectasis
- Completes QOL-B
- NTM Module
  - NTM Module + Additional Scales
    - Digestive Symptoms
    - Eating Issues
    - NTM Symptoms

CF
- Completes CFQ-R
  - CFQ-R contains Body Image, Digestive Symptoms, & Eating Issues Scales
  - Only fill out NTM Module
Summary & Future Directions

• Cognitive testing indicated that the draft items were relevant, clear, and easy to understand

• Very good reliability

• When utilizing NTM module with bronchiectasis: use module + Body Image, Eating Issues, & Digestive Symptoms scale?

• Need more data!
Summary & Future Directions

- Next steps include additional psychometric testing, and identification of meaningful change.
- Insmed has agreed to perform extensive psychometric analyses on their baseline clinical trial:
  - Reliability
  - Convergent validity: medical characteristics, microbiology, SGRQ, 6-minute walk
Acknowledgements

Funding from Insmed and NTMIR for initial, qualitative data collection

Input from patients across the US!

Input from a NY support group (thank you Katie Keating!)

Expert physicians who have provided input and assisted with data collection